a. The specification

The specification has been amended to update the status of the related applications. The specification has been amended to include a sequence listing containing nucleotide and amino acid sequences referred to elsewhere in the specification.

b. The claims

New claims 46-49 have been added. Pursuant to 37 C.F.R. § 1.607(c), Applicants identify these claims as corresponding to claims 1, 13, 14 and 18 of U.S. Patent No. 6,114,148, respectively, as demonstrated by the chart below:

Seed U.S. 6,114,148 (issued 9/5/00)	**New Claims 46-49**
1. A synthetic gene encoding a protein normally expressed in an eukaryotic cell wherein at least one nonpreferred or less preferred codon in a natural gene encoding said protein has been replaced by a preferred codon encoding the same amino acid, said synthetic gene expressing said protein at a level which is at least 110% of that expressed by said natural gene in an in vitro mammalian cell culture system under identical conditions.	46. A synthetic gene encoding a protein normally expressed in an eukaryotic cell wherein at least one rarely-used or less preferred codon in a natural gene encoding said protein has been replaced by a preferred codon encoding the same amino acid, said synthetic gene expressing said protein at a level which is higher than that expressed by said natural gene in an in vitro mammalian cell culture system under identical conditions.
13. An expression vector comprising the synthetic gene of claim 1.	47. An expression vector comprising the synthetic gene of claim 46.
14. A mammalian cell which harbors the synthetic gene of claim 1.	48. A mammalian cell comprising the synthetic gene of claim 46.
18. A method for preparing a synthetic gene encoding a protein normally expressed by mammalian cells, comprising identifying non-preferred and less-preferred codons in the natural gene encoding said protein and replacing one or more of said non-preferred and less-preferred codons with a preferred codon encoding the same amino acid as the replaced codon, so that a synthetic gene is prepared.	49. A method for preparing a synthetic gene encoding a protein normally expressed by mammalian cells, comprising identifying rarely-used and less-preferred codons in the natural gene encoding said protein and replacing one or more of said rarely-used or less-preferred codons with a preferred codon encoding the same amino acid as the replaced codon, so that a synthetic gene is prepared.

See also, Seed U.S. Patent Nos. 5,786,464 and 5,795,737 for related claims.

Claim 46 is directed to

A synthetic gene encoding a protein normally expressed in an eukaryotic cell wherein at least one rarely-used or less preferred codon in a natural gene encoding said protein has been replaced by a preferred codon encoding the same amino acid, said synthetic gene expressing said protein at a level which is higher than that expressed by said natural gene in an in vitro mammalian cell culture system under identical conditions.

Claims 47 and 48 are directed to an expression vector and mammalian cell,

respectively, comprising the synthetic gene of claim 46. Claim 49 is directed to

> a method for preparing a synthetic gene encoding a protein normally expressed by mammalian cells, comprising identifying rarely-used and less-preferred codons in the natural gene encoding said protein and replacing one or more of said rarely-used or less-preferred codons with a preferred codon encoding the same amino acid as the replaced codon, so that a synthetic gene is prepared.

Support for new claims 73-76 can be found throughout the specification. See, e.g., p. 9, lines 20-23, for support for synthetic genes and expression vectors and host cells containing these genes. See also, e.g., p. 39, line 32 to p. 40, line 6. Support for genes encoding a protein normally expressed in an eukaryotic cell can be found, e.g., on p. 22, lines 27-35; p. 23, lines 3-6; and p. 40, lines 28-32, which describe examples of genes, including the eukaryotic "cellular" genes listed therein. Support for mutating a gene by replacing rarely-used or less-preferred codons with preferred codons encoding the same amino acid can be found, e.g., at p. 20, lines 15-17; p. 20, lines 31-33; p. 21, lines 17-19; p. 33, lines 22-24 and 27-29; p. 36, line 26 to p. 37, line 7; and Example 1.

Support for expressing the protein from the mutated gene at a level which is higher than that expressed by the natural gene in vitro in mammalian cell culture under identical conditions is found, e.g., on p. 26, line 7; p. 41, lines 6-9; p. 40, lines 14-23; p. 14, lines 17-27; and in Example 1 and Figure 2.

Applicants respectfully submit that the above amendments do not constitute new matter and respectfully request entry thereof.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendment and an action passing this case to issue is therefore respectfully requested.

Respectfully submitted,

MORGAN & FINNEGAN, L.L.P.

Dated: August 31, 2001

By: 
Mary J. Morry
Registration No. 34,398

Mailing Address:
MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, New York 10154
(212) 758-4800 Telephone
(212) 751-6849 Facsimile

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification (on page 1):

-- This application is a continuation of 09/678,437 filed October 2, 2000, which is a continuation of U.S. Serial No. 09/414,117, filed October 8, 1999, which is a continuation of U.S. Serial No. 08/850,049, filed May 2, 1997 (now U.S. Patent 5,965,726), which is a continuation of U.S. Serial No. 08/050,478, filed October 26, 1994 (now U.S. Patent 5,972,596), which is in turn a continuation of the National Stage under 35 U.S.C. §371 of PCT/US93/02908, filed March 29, 1993, which is in turn a continuation-in-part of U.S. Serial No. 07/858,747, filed March 27, 1992 (now U.S. Patent 6,174,666 B1). The disclosures of each of these applications is hereby incorporated by reference. -- [This application is a continuation-in-part of U.S. Serial No. 07/858,747, filed March 27, 1992.]

In the claims:

46. (New) A synthetic gene encoding a protein normally expressed in an eukaryotic cell wherein at least one rarely-used or less preferred codon in a natural gene encoding said protein has been replaced by a preferred codon encoding the same amino acid, said synthetic gene expressing said protein at a level which is higher than that expressed by said natural gene in an in vitro mammalian cell culture system under identical conditions.

47. (New) An expression vector comprising the synthetic gene of claim 46.

48. (New) A mammalian cell comprising the synthetic gene of claim 47.

49. (New) A method for preparing a synthetic gene encoding a protein normally expressed by mammalian cells, comprising identifying rarely-used and less-preferred codons in the natural gene encoding said protein and replacing one or more of said rarely-used or less-

preferred codons with a preferred codon encoding the same amino acid as the replaced codon, so that a synthetic gene is prepared.